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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/589,287	06/08/00	YU G	PF343P3C1

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HM12/1106

EXAMINER	
PRASAD,S	
ART UNIT	PAPER NUMBER
1646	7

DATE MAILED: 11/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/589,287	YU ET AL.	
	Examiner	Art Unit	
	Sarada C Prasad	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,17 and 26-250* is/are pending in the application.

4a) Of the above claim(s) *1 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-250* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Action

1. Applicant's election with traverse of Group III in Paper No. 6 (8/17/01) is acknowledged. Original claims 2-16, 18 and 18-25 have been cancelled and new claims 26-250 have been added. Currently, claims 1,17, 19, and 26-274 are pending.

The traversal is on the ground(s) that a search of the polynucleotide claims would clearly provide useful information for the polypeptide claims and a search of the polypeptide claims, as a matter of routine, would include a search for antibodies, and hence restriction of original claims 1-25 to Groups I, II, III is not proper. This is not found persuasive because the inventions of Groups I, II and III, directed to polynucleotide, polypeptide, and antibodies are distinct as noted in the last Office Action, and as shown by the distinctness described therein. Applicant's attention is directed to MPEP 806.05. Contrary to Applicants' assertion that any search of the prior art in regard to Group I would reveal whether any prior art exists as to the other inventions of Groups II and III, the search is in fact directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a focussed search of relevant literature in many different areas of subject matter. Furthermore, divergent classification of the three Groups of inventions I-III has been an additional criterion for the restriction of the claims 1-26 into three distinct inventions. Each of these inventions would require non-cohesive classification searches posing an undue burden for the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Currently, claims 26-250 are under consideration.

Specification

2a. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

2b. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. A suggested title would be 'Antibodies to neutrokine-α'.

Claim Rejections - 35 USC § 112-First paragraph-Scope of enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 26-250 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibody or portion thereof that specifically binds to full length amino acid sequence of SEQ ID NO. 2, does not reasonably provide enablement for an isolated antibody or portion thereof that specifically binds to fragments, derivatives, fusion peptides, variants, or C-terminal or N-terminal deletion mutants of SEQ ID NO.2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Issues that are addressed in the rejection are

(a) an isolated antibody that specifically binds to a full length polypeptide of SEQ ID No.2 and (b) other isolated antibodies that specifically bind to fragments, derivatives, or selected portions of the amino acid sequence of SEQ ID No. 2.

What does the specification set forth:

The specification sets forth general methods for preparation of (a) epitope bearing peptides (starting at 2nd para on page 113, until 1st para on page117) that constitute various lengths of antigenic regions covering the entire 1-285 amino acid long sequence of SEQ ID NO.2; (b) antibodies to these various derivatives of SEQ ID No. 2 for use as antagonists (page 24, 3rd para, lines 5-6); and (c) various antibody derivatives or portions thereof containing the antibody binding site (Fab fragments), or antibodies amenable to use in human beings (chimeric, humanized, fusion proteins with detection tags) in pages 228-261. However, very few specific examples of such 'contemplated antibodies directed to specific regions of SEQ ID NO. 2' are disclosed (Examples 9 and 10, pages 427-433). In particular, Example X shows screening of 729 hybridomas, with 23 positive for detectable antibody to SEQ ID No. 2. Only two real world antibodies, one that was observed to neutralize neutrokine-α receptor interaction, and another that can bind both soluble and membrane bound forms of the neutrokine-α are demonstrated (antibody termed 15C10 in page 432, 4th and 5th paragraphs).

The instant specification is only enabled for an isolated antibody or portion thereof that specifically binds to a full length amino acid sequence of SEQ ID NO. 2 but not for an isolated antibody or portion thereof that specifically binds to fragments, derivatives, fusion peptides,

variants, or C-terminal or N-terminal deletion mutants of SEQ ID NO.2, or a full length protein encoded by the cDNA contained in ATCC deposit Number 97768, or portions of that protein.

Therefore, recitation of (i) an isolated antibody that specifically binds to a protein consisting of an amino acid sequence of amino acid residues 1-285 of SEQ ID No.2; or an isolated antibody to a fragment of SEQ ID NO. 2 wherein the fragment comprises an amino acid sequence of at least 9 contiguous amino acid residues of SEQ ID NO.2; or an isolated antibody to a fragment of SEQ ID No.2 comprising an amino acid sequence 115-147 or 150-163, 171-194, or 223-247 or 271-278 of SEQ ID No.2;

(ii) an isolated antibody that specifically binds to amino acid residues 73-285 of SEQ ID No.2, or

(iii) an isolated antibody that specifically binds to amino acid residues 134-285 of SEQ ID No. 2, or

(iv) an isolated antibody that specifically binds to a protein consisting of an amino acid sequence of amino acid residues n-285 of SEQ ID No. 2 where n is an integer in the range of 2-190; or to amino acid residues 1-m of SEQ ID NO. 2 where m is an integer in the range of 274-284; or to amino acid residues n-m of SEQ ID NO.2 where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

(v) an isolated antibody to a full length protein encoded by the cDNA contained in ATCC deposit number 97768;

(vi) an isolated antibody that specifically binds to the extracellular domain of the protein encoded by the cDNA contained in ATCC deposit number 97768;

(vii) an isolated antibody that specifically binds to the amino acid sequence of an amino terminal deletion protein mutant of the full length protein encoded by the cDNA contained in ATCC deposit number 97768, wherein said amino terminal deletion protein mutant excludes up to 190 residues from the amino terminus of said full length protein encoded by the cDNA contained in ATCC deposit number 97768;

(v) an isolated antibody that specifically binds to the amino acid sequence of a carboxy terminal deletion protein mutant of the full length protein encoded by the cDNA contained in ATCC deposit number 97768, wherein said carboxy terminal deletion mutant excludes up to 11 amino acid residues from the carboxy terminus of said full length protein encoded by the cDNA contained in ATCC deposit number 97768;

(vi) the amino acid sequence of an amino and carboxy terminal deletion protein mutant of the full length protein encoded by the cDNA contained in ATCC deposit number 97768, wherein said amino and carboxy terminal deletion protein mutant excludes up to 190 amino acids from the amino terminus and up to 11 residues from the carboxy terminus of said full length protein encoded by the cDNA contained in ATCC deposit number 97768, wherein the peptide sequence modulates lymphocyte proliferation,

in claims 26, 47, 68, 92, 113, 136, 162, 183, 204, 228 is very broad.

Analyses of why the instant claims are rejected based on their broad scope:

The Numerous antigenic regions of SEQ ID No. 2 are contemplated, but not really disclosed as having generated antibodies with the said specificities:

Claims reciting isolated antibodies the numerous fragments of SEQ ID NO.2 with hypothetical amino acid delimiters, N-terminal and C-terminal deletion mutants as being

immunogenic are not supported by the specification because the various antigen specificities are contemplated and not real world. Instant specification fails to provide what is the specificity of the numerous contemplated antibodies to the numerous contemplated antigenic/epitopic regions. For example: both polyclonal and individual monoclonal antibodies raised using full length SEQ ID NO.2 would be directed to various stretches of antigenic regions of SEQ ID No. 2. It is not feasible for a skilled artisan to state that any one of such antibodies specifically binds to which of the 1-285 residues of SEQ ID NO.2 unless each of these antibodies is characterized. The Example X shows that there is one such antibody that has been disclosed in the instant specification, 15C10 (page 432, 4th and 5th paragraphs). However, guidance is not provided as to what was the immunogen/antigen that resulted in generation of this particular antibody, what was the neutrokine-α response that was inhibited, other than mention that this antibody was able to neutralize the binding of neutrokine-α to its receptor. In fact, with the state of the art techniques describing antibodies to epitopes as short as tripeptides, there is no one isolated antibody that specifically binds to the entire length of polypeptides. Additionally, inhibition of lymphocyte proliferation is the expected end point of the inhibition of neutrokine-α receptor interaction. In spite of the many antibodies that have been contemplated, the specification fails to provide such information of the potential of the different antibodies or comparison of the specific binding of antibodies directed to full length polypeptide to those directed to portions of the polypeptide. In fact, several of the contemplated immunogens of SEQ ID NO. 2 consist of amino acid sequences randomly selected with 'n' amd 'm' as the delimiting amino acid residues. Epitope bearing regions of the polypeptide are not distributed randomly in that fashion. In the instant case, the Applicant is asking for lisence to perform futher experimentation to check and identify antigenic

regions that have been suggested by biophysical methods. In order to fulfill the enablememt requirement, the application has to be complete at the time of submission and not later.

See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Given the breadth of claims reciting antibodies to fragments, derivatives, deletion mutants of SEQ ID No. 2, in light of the predictability of the art that epitope bearing regions are not randomly distributed all over the sequence, as determined by the lack of working examples showing that the envisioned antibodies to the various epitope berating regions of SEQ ID No. 2 do have the expected specificity and utility, state of the art suggesting how guidance is needed for a skilled artisan for each and every specific antibody, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 27-46, 48-67, 69-91, 93-112, 114-135, 137-161, 163-182, 184-203, 205-227, 229-250 are rejected insofar as they depend on claims 26, 47, 68, 92, 113, 136, 162, 183, 204, 228.

Conclusion

4. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday - Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.
Examiner
Art Unit 1646
November 2nd, 2001

Yvonne Eyler
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SUPERVISORY PATENT EXAMINER
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